REMARKS

Claims 1-13 and 18-23 are in the application. Claims 18 and 23 remain withdrawn from consideration.

Rejection under 35 USC §112, First Paragraph, Scope of Enablement

Claims 1-13, and 19-22 remain rejected under 35 USC §112, first paragraph, as failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

The previous enablement rejection was presented slightly different in that the Examiner found the specification "being enabling for the compounds of Formula (I), but not being enabling for "use of the same". Applicants presume this remains the same rejection.

There is a legal requirement that the compounds possess at least one credible utility. At the time of filing of this application, there are quite a few art recognized p38 mediated diseases for which inhibition of the kinase would be useful. There has been several proof of concept (POC) studies performed by Applicants as well as others in this field. Looking at the ClnicalTrials.gov database with the key term of p38 (http://clinicaltrials.gov/ct2/results?term=p38) retrieves 34 studies, although not all were started prior to the filing date of this application. Applicants also attach another publication, from 2002, on a structurally unrelated p38 inhibitor which also clearly demonstrates the state of the art and the linkage to inhibition of the p38 MAP kinase (as well as the usage of a similar fluorescent binding assay as Applicants). See Regan et al., J. Med Chem., 45, pg 2994-3008 (2002).

Applicants maintain that their specification clearly contains sufficient information on how to "use". See pages 22, lines 1 to 42 – page 32, lines 1 -11. In the Specification, pages 107, lines 35 to 41 – pages 110, lines 1 – 23 teach suitable assays to determine biological activity.

The Examiner appears not to recognize that actual biological data is presented in a relevant biological model, contrary to the Examiner's assertion. However, it should be noted that there is no legal requirement to provide such actual data in the specification.

The compounds of the Examples (i.e. compounds of Formula (I), "were tested in at least one of these noted assays and had either IC_{50} values of <10 μM or pKi values of >6", as shown on page 110, lines 22 and 23. Applicants assert that these assays are art recognized assays for determining inhibitory activity of a compound against the p38 kinase. It is also well established in the art that the inhibition of the p38 kinase and the linkage of that inhibition to the various cited diseases (and the inflammatory component of those diseases) is also known. The Examiner is suggested to consult the many references previously forwarded to the USPTO for such linkages.

The Examiner comments that this is "… not persuasive. The assay simply leads to the conclusion that binding in fact occurs. The assay does not lead the conclusion that this binding is null, inhibitory or activating". (See page 8, 1rst ¶). The Examiners is is incorrect on this point. The skilled artisan would readily recognize that this assay teaches a level of binding affinity for the enzyme and that one would be able to determine whether a compound was sufficiently active (as an antagonist) in the assay to be of use clinically. This is not a new assay, it is a standard screening assay in the industry as can readily be seen be the paper submitted herewith, as well as the many filed patent applications, and significant number of publications in this field.

This is not the first filed p38 kinase application filed. Applicants were, however, the first to find and to file patent applications on the kinase. Applicants have been filing applications since the mid-90's in this field. Large numbers of competitors have also been filing compound and method of use cases in this field for many years as well, with a number of potential candidate compounds tested in humans.

The signaling pathway of p38 kinase has been extensively studied. As noted Applicants have provided quite a bit of information on the utility of p38 inhibitors for treatment for a wide range of diseases, including inflammation. It is well established in the art that there is a correlation of p38 inhibition and its affect on the pro-inflammatory cytokine cascade. Consequently, Applicants believe that they have provided sufficient grounds of enablement for the compounds of Formula (I) as described herein.

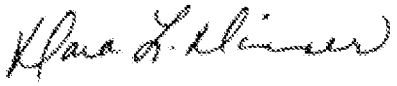
Applicants respectfully submit that the originally filed disclosure provides more than sufficient information on how to use, how to formulate, how to dose, and how to administer the compounds of Formula (I). Based on this, Applicants maintain that the specification is sufficiently enabled and would not require undue experimentation to practice the invention.

In view of these remarks and amendments reconsideration and withdrawal of the rejection to the claims under 35 USC §112, first paragraph is respectfully requested.

CONCLUSION

Should the Examiner have any questions or wish to discuss any aspect of this case, the Examiner is encouraged to call the undersigned at the number below. If any additional fees or charges are required by this paper, the Commissioner is hereby authorized to charge Deposit account 19-2570 accordingly.

Respectfully submitted,



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